REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the following reasons.

I. Status of the Claims

Claims 73 and 74 are added with exemplary support in the original specification, e.g., at page 6, lines 16 and 23. Because no new matter is introduced, Applicants respectfully request entry of this amendment. Upon entry, claims 28-36, 39-40, 42-43, 51-60 and 64-74 are pending.

II. Rejection of Claims under 35 U.S.C. §103(a)

A. Rejection of Claims 28-36, 39-40, 51-60 and 64-72

Claims 28-36, 39-40, 51-60 and 64-72 are rejected under 35 U.S.C. §103(a) for allegedly being obvious over U.S. Patent No. 5,145,684 to Liversidge et al. ("Liversidge") in view of Pavord et al., *Clin. Pharmacokinetc.*, *25*(2): 126-135 (1993), abstract ("Pavord"), Glaxo History available at http://www.gsk.com/about/history-noflash.htm ("Glaxo History"), and the Merck Index, 10th ed., page 144, entry 1018 ("the Merck Index"), as evidenced by U.S. Patent No. 5,049,389 to Radhakrishnan et al. ("Radhakrishnan") and U.S. Patent No. 5,208,226 to Palmer et al. ("Palmer"). Applicants respectfully traverse the rejection.

(1) The Examiner fails to meet the initial burden to establish a *prima facie* case of obviousness.

The Examiner asserts that although Liversidge does not teach the specific active agent, the deficiency is cured by the secondary references, Pavord, Merck Index, and Glaxo History, as evidenced by Radhakrishnan and Palmer. Applicants respectfully disagree because Liversidge not only fails to teach the specific active agent, but also fails to teach an aerosol formulation. This is significant as Applicants' claimed invention is directed to a method of treating a

respiratory illness in a mammal comprising administering an aerosol composition of an aqueous dispersion of a nanoparticulate active agent.

The Examiner cites Glaxo History and contends that it would be obvious to obtain aqueous suspensions of beclomethasone because Becotide® is a commercially available aqueous suspension of beclomethasone sold by Glaxo. *See* Office Action, page 8, lines 12-16. Glaxo History contains only a one-sentence disclosure of Becotide®, excerpted below:

> *1972*
>
> *Scientists at Beecham Research Laboratories discover amoxicillin and launch* Amoxil, *to become a widely-used antibiotic. Beecham Group plc is unsuccessful in its bid for Glaxo Group Ltd - and Glaxo is unsuccessful in its attempt to merge with UK chemists Boots. Inhaled steroid beclomethasone dipropionate is launched by Glaxo as* Becotide *(beclomethasone dipropionate) for asthma, followed in 1975 by* Beconase *for rhinitis conditions.*

In view of the disclosure by Glaxo History, the skilled artisan would not have any guidance from the art as to how to develop an aerosol formulation of beclomethasone, let alone finding any connection between the particle size of beclomethasone and developing optimal aerosol formulation. Applicants further submit Exhibit A, an excerpt from http://www.drugs.com/international/becotide.html, to demonstrate that Becotide® was never marketed in the U.S. Accordingly, the Examiner has failed to establish a *prima facie* case of obviousness.

(2) The claimed invention is nonobvious in view of the unexpected results evidenced by an inventor's declaration.

In the Office Action, the Examiner challenged the Bosch Declaration filed on August 30, 2010, by alleging the following defects: (i) the Declaration fails to present data to compare the allegedly closest art of Liversidge, (ii) the claims are not limited to a particular surface stabilizer

or a particular concentration of the surface stabilizer, and (iii) the Declaration fails to disclose the beclomethasone particle size of the formulations.

In response to point (i), Applicants respectfully submit that Applicants should not be required to compare the claimed invention with the compositions of Liversidge. This is because, contrary to the Examiner's assertion, one of ordinary skill in the art would not consider Liversidge to be the closest art. Liversidge discloses a nanoparticulate active agent composition in general but fails to disclose beclomethasone as the active agent. In other words, the nanoparticulate beclomethasone composition is NOT a prior-art product but Applicants' own invention. The Examiner did not prove that such a product existed in the art, but rather relied on a combination of the cited references to attempt a rejection for alleged obviousness. Therefore, it is impossible for Applicants to submit data to compare with an imaginary product which did not exist at the time of the invention.

Moreover, Liversidge is not the closest art to the claimed invention because Liversidge is silent as to an aerosol formulation of a nanoparticulate active agent dispersion, which is required by the claimed invention. Rather, the Drug Information Handbook cited by the Examiner identifies several commercial formulations of beclomethasone dipropionate marketed under the trademarks Beclovent®, Beconase®, Beconase AQ®, Vancenase AQ®, Vanceril®. *See* page 95, entry "Beclomethasone Dipropionate."

In the accompanying Declaration executed by Dr. Bosch, Applicants submit additional data comparing the delivery efficiency between Vanceril® and the claimed aerosol of a nanoparticulate beclomethasone dipropionate composition. As demonstrated by the Declaration, the claimed aerosol of a nanoparticulate beclomethasone dipropionate composition unexpectedly exhibited superior delivery efficiency in terms of increased respirable dose and decreased throat deposition. *See* the Declaration, Tables 4 and 5, and paragraphs 14 and 17. Applicants respectfully request that the Examiner give full consideration to the rebuttal evidence.

Regarding point (ii), Applicants submit additional evidence for another formulation encompassed by the claimed invention, which comprises tyloxapol as the surface stabilizer. This additional evidence demonstrates that the aerosol beclomethasone composition encompassed by Applicants' claims unexpectedly exhibited superior delivery efficiency in comparison with a non-nanoparticulate commercial beclomethasone aerosol formulation. *See* the Declaration, section III.

Pursuant to MPEP 2145, Applicants are not required to show unexpected results for the entire claimed genus.

> *When considering whether proffered evidence is commensurate in scope with the claimed invention, Office personnel should not require the applicant to show unexpected results over the entire range of properties possessed by a chemical compound or composition. See, e.g., In re Chupp, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987). Evidence that the compound or composition possesses superior and unexpected properties in one of a spectrum of common properties can be sufficient to rebut a prima facie case of obviousness. Id.*
>
> *For example, a showing of unexpected results for a single member of a claimed subgenus, or a narrow portion of a claimed range would be sufficient to rebut a prima facie case of obviousness if a skilled artisan "could ascertain a trend in the exemplified data that would allow him to reasonably extend the probative value thereof." In re Clemens, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980) (Evidence of the unobviousness of a broad range can be proven by a narrower range when one skilled in the art could ascertain a trend that would allow him to reasonably extend the probative value thereof.).*

Accordingly, new claims 73 and 74 are nonobvious in view of the unexpected results demonstrated by the Declaration.

Turning to point (iii), the Declaration submitted herewith includes particle size information for all formulations tested.

In view of the foregoing, Applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. §103(a).

B. Rejection of Claims 42-43

Claims 42-43 are rejected under 35 U.S.C. §103(a) for allegedly being obvious over Liversidge in view of Pavord, Glaxo History, and the Merck Index, as evidenced by Radhakrishnan and Palmer, and further in view of U.S. Patent No. 5,525,623 to Spear et al. ("Spear"). Applicants respectfully traverse the rejection.

The primary and secondary references are discussed in the foregoing paragraph. Spear is cited for the alleged teaching of a jet nebulizer or an ultrasonic nebulizer but fails to compensate for the deficiencies of the primary and secondary references, as discussed above. Therefore, claims 42 and 43 are nonobvious for depending from a nonobvious base claim.

Moreover, the Bosch Declaration submitted herewith demonstrates that the claimed aerosol of a nanoparticulate beclomethasone dipropionate composition delivered by an ultrasonic nebulizer exhibited superior delivery efficiency in comparison to Vanceril® delivered by a propellant-based MDI. Therefore, the dependent claims benefit from additional ground of patentability in view of the unexpected results.

III. Provisional Double Patenting

Claims 28-33, 39-40, 51-60, 66, 69 and 72 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-7, 9-11, and 13-14 of copending Application No. 10/035,324 ("the '324 application") in view of Liversidge and Radhakrishnan.

Claims 28-33, 53-60, 66, 69 and 72 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 60-61, 64-65, 69-70 and 72-76 of copending Application No. 10/768,194 ("the '194 application") in view of Liversidge and Radhakrishnan.

Finally, claims 28-36 and 51-60 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-11 and 17-18 of copending Application No. 12/292,092 ("the '092 application") in view of Liversidge and Radhakrishnan. Applicants respectfully traverse each rejection.

The present application was filed on May 25, 2000; whereas the copending '324 application entitled "Sterile Filtered Nanoparticulate Formulations Of Budesonide And Beclomethasone Having Tyloxapol As A Surface Stabilizer" was filed on January 4, 2002. In addition, the copending '194 application entitled "Novel Fluticasone Formulations" was filed on February 2, 2004, and the copending '092 application entitled "Nanoparticulate Compositions Of Immunosuppressive Agents" was filed on November 12, 2008.

Pursuant to MPEP 804, "[i]f a "provisional" nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer."

Accordingly, the present earlier-filed application should be allowed to proceed to allowance should the Examiner withdraw the other rejection of the claims.

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to

Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date: March 31, 2011

By _____

FOLEY & LARDNER LLP
Customer Number: 31049
Telephone: (202) 672-5538
Facsimile: (202) 672-5399

Michele M. Simkin
Attorney for Applicant
Registration No. 34,717